UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,864	02/07/2005	Dorothea Gross	P30,365 USA	1876

23307 7590 07/19/2007

SYNNESTVEDT & LECHNER, LLP
1101 MARKET STREET
26TH FLOOR
PHILADELPHIA, PA 19107-2950

EXAMINER	
HUANG, GIGI GEORGIANA	
ART UNIT	**PAPER NUMBER**
1618	

MAIL DATE	DELIVERY MODE
07/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/523,864	GROSS ET AL.	
	Examiner	Art Unit	
	GiGi Huang	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Non-Final Rejection

1. Claims 1-9 are present for examination at this time.

Claim Rejections - 35 USC § 112

2. Claims 1-9 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to ophthalmologic dysfunctions linked to or attributed to circulatory disturbances of the eye. Thus, the claims taken together with the

specification imply that every condition where there is any dysfunction or any circulatory disturbance would apply. This would read on glaucoma, diabetic retinopathy, and also any wound or wound healing as that is an ophthalmologic dysfunction linked to or attributed to circulatory disturbances of the eye.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

The state of the prior art addresses the use of papaverine to inhibit smooth muscle contraction in the eye to promote wound healing. This is applicable as to show that papaverine is known for ophthalmic use in ophthalmologic dysfunctions that have circulatory disturbances in the broadest interpretation of the claims.

However, the prior of Steinbach et al. (Wirkung gefaBerweiternder Substanzen auf Anugeninnendruck und Blutdruck -The Influence of Vasodilators of Intraocular Pressure and Blood Pressure, Graefes Archiv Opthalmologie) teaches the use of several vasodilators including moxaverine (Eupaverin) for glaucoma, a circulatory disturbance to the eye common with diabetes and diabetic retinopathy (see sheets from American Diabetic Association and sheets from Glaucoma Research Foundation).

Note that the page and section references for Steinbach et al. (Wirkung gefaBerweiternder Substanzen auf Anugeninnendruck und Blutdruck -The Influence of Vasodilators of Intraocular Pressure and Blood Pressure, Graefes Archiv Opthalmologie) are based on the translation provided.

Steinbach et al. teaches that the use of moxaverine reduced blood pressure initially then rose above the starting blood pressure.

Steinback also taught that there was ***always*** a rise in intraocular pressure, which is not desirable in ocular vascular disturbances and intraocular pressure conditions such as glaucoma or retinopathy. The results of vasodilator therapy in eyes with increase intraocular pressure (glaucoma) were the following: for patients with normal systemic blood pressure the therapy was "***useless***" since perfusion pressure would counter the decrease by the vasodilators; for patients with high blood pressure, the prognosis was ***unfavorable*** in terms of ocular circulation, the exception was prior to eye-opening surgery were the pressure would be reduced and would not have a possible ***vessel rupture***; for patients with low blood pressure, the vasodilators were ***absolutely contraindicated as the probability of vascular collapse with ischemia in the ocular nerve head was large*** (Page 2, Introduction, Page 5, Results, Page 7, Eupaverin (moxaverine), Page 12, Group B: High intraocular pressure, Page 13).

The object of the instant invention is the treatment of circulatory disturbances of the eye due to diabetes, specifically glaucoma and diabetic retinopathy with of moxaverine, papaverine, ethaverine, elziverine, and its salts or mixtures. The invention is not enabled as Steinbach et al. shows an increase in intraocular pressure in the administration of moxaverine, which would actually worsen the existing high intraocular pressure and worsen the glaucoma and possibly even rupture the fragile abnormal and leaking blood vessels found in retinopathy creating greater blood spills in the eye.

Thereby the level of unpredictability is very high and as evidenced by Steinbach et al., the use of moxaverine and papaverine-like compounds are contraindicated for a number of dysfunctions linked to or attributed to diabetes.

A species can anticipate a genus as evidenced by moxaverine, but a genus cannot anticipate a species.

Thereby, the use of moxaverine and vasodilators with identical chemical core structure/function (papaverine, ethaverine, elziverine, and the salts or mixtures) would also not be enabled for glaucoma or any other circulatory disturbance subject to increased pressure such as retinopathy, as they are all in the same genus and the common core is what dictates the activity of the drugs.

(5) The relative skill of those in the art:

The relative skill of those in the art is high.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for ophthalmologic dysfunction to be from the group consisting of glaucoma, neovascularization glaucoma, hemorrhagic glaucoma, and diabetic retinopathy.

However, the specification does not provide any working examples exemplifying whether the invention is enabled. Absent any evidence to the contrary, the prior art teaches away from the use of the moxaverine, papaverine, ethaverine, elziverine, and its salts or mixtures for the dysfunctions listed above. The specification only provides example of increased concentration of moxaverine present in the conjunctiva, cornea, iris, ciliary process, and retina. This does not show any measure of the intraocular pressure. This is a critical point as any increase in intraocular pressure in any of the

dysfunctions would lead to the final endpoint in the progression of the conditions listed when uncontrolled: blindness.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to the enablement for the dysfunctions selected in the specification and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

It is noted that topical treatment for diabetic retinopathy is not currently enabled as shown by the American Diabetic Association, the treatment for retinopathy are scatter photocoagulation, focal photocoagulation, and vitrectomy (see sheets from American Diabetic Association).

It is noted that topical treatment for neovascular glaucoma is not currently enabled as shown by the Glaucoma Research Foundation, the treatment for neovascular glaucoma are laser surgery and drainage implants (see sheets from Glaucoma Research Foundation).

All the critical elements are taught by the cited reference and thus the claims are rejected.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "papaverine-like" is indefinite as it is unclear what the metes and bound of the invention are. The term is unclear as to how similar to papaverine the vasodilator must be. It could be similar to papaverine in terms of activity level, in terms of similar structure, in terms of effect, or it could be any vasodilator. As a result, the term is indefinite and does not allow for one of skill in the art to determine the metes and bounds of the invention

All the critical elements are taught by the cited reference and thus the claims are rejected.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Schacher (U.S. Pat. No. 4390542).

Schacher teaches the use of papaverine for controlling the contraction of ophthalmic wound or incisions to promote healing. This is accomplished by relaxing the smooth muscles of the eye (thereby inhibiting contraction) to overcome repeated contraction (tearing and separation of wound edges) and regression of the cornea from the desired configuration. Thereby inhibition of smooth muscle contraction in the eye promotes wound healing. This is applicable as to show that papaverine is known for

ophthalmic use in ophthalmologic dysfunctions that have circulatory disturbances in the broadest interpretation of the claims. This is would be an inherent property when applied to any patient population including diabetics where delayed wound healing is well known (see Diabetologia sheets) and where promotion of corneal healing is necessary.

Schacher also teaches that the method of delivery is topically applied in a suitable, non-toxic ophthalmic vehicle such as eye drops and ointments. The vehicle comprised of buffers biocides, and viscosity building agents including natural gums, starch derivatives, polymeric glycols, and cellulose polymers (Abstract, Col. 1, lines 5-20, 45-60, Col. 2, lines 6-14, 19-25, 39-48, 59-64, Col. 3, lines 3-19, 24-28, Col 4, lines 1-8, Claims 1-5).

A species can anticipate a genus as evidenced by papaverine, but a genus cannot anticipate a species.

Thereby, the use of papaverine and vasodilators with identical chemical core structure/function (moxaverine, ethaverine, elziverine, and the salts or mixtures) would have the same inherent properties as papaverine for contraction inhibition, as they are all in the same genus and the common core is what dictates the activity of the drugs.

All the critical elements are taught by the cited reference and thus the claims are anticipated.

Conclusion

6. Claims 1-9 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GiGi Huang whose telephone number is (571) 272-9073. The examiner can normally be reached on Monday-Thursday 8:30AM-6:00PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GH

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER